Consideration of Endocrine-Mediated Mode of Action and Life Stage–Specific Susceptibility in the Risk Assessments for Two Pesticides

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Historically, the Office of Research and Development (ORD) has contributed to the risk assessments of specific individual pesticides or classes of pesticides through test methods development, the generation of data, and consultation with the Office of Pesticide Programs (OPP). Recent research, supported by the Endocrine Disruptor Chemicals (EDC) Program, focused on determining the mode of action (MOA) for two widely used pesticides, atrazine and vinclozolin, that were being evaluated by OPP for re-registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), including an assessment of potential risks to children, as mandated by the Food Quality Protection Act (FQPA). The effort included carefully characterizing the toxicity pathways that these pesticides acted through and subsequently determining the effects of exposure across varying life stages (e.g., prenatal, postnatal, peri-pubertal, and adult).

In the case of atrazine, seminal research was conducted by the National Health and Environmental Effects Research Laboratory (NHEERL) scientists to identify the critical non-cancer MOA for risk assessment, that is, disruption to the hypothalamic–pituitary–gonadal axis during development. For vinclozolin, NHEERL research was instrumental in developing sensitive biomarkers of adverse effects for anti-androgenic substances administered during development. The anti-androgenic MOA was characterized for vinclozolin, and the dose–response profile was identified for critical developmental and reproductive effects related to this MOA. Overall, for both atrazine and vinclozolin, ORD studies provided methodologies to assess hazard, confirmation of susceptibility during specific life stages, support for decisions regarding the adverse consequences of the observed effects, a basis for extrapolation from animal data to potential human response, and information critical in identifying the point of departure for risk assessments conducted by OPP.

For atrazine and vinclozolin, risk management decisions made by OPP addressed the protection of susceptible populations in relation to the critical endocrine-mediated MOA. For atrazine, risk communication efforts were critical in refocusing public perception of potential risks away from long-term cancer concerns (the focus of past risk assessments) and toward non-cancer endocrine-mediated risks to susceptible populations. For vinclozolin, data generated by ORD were utilized in establishing endpoints and doses for short- and intermediate-term, non-dietary risk assessments and for characterizing remaining data gaps and uncertainties. Additionally, characterization of risks associated with vinclozolin exposures during development resulted in risk mitigation actions (cancellation and/or limitation of specific uses to reduce potential exposures to children).

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